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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,454	07/10/2007	Kozo Ninomiya	P30320	4690

7055 7590 08/07/2008

GREENBLUM & BERNSTEIN, P.L.C.
1950 ROLAND CLARKE PLACE
RESTON, VA 20191

EXAMINER	
GOON, SCARLETT Y	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
08/07/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com
pto@gbpatent.com

Office Action Summary	Application No.	Applicant(s)	
	10/586,454	NINOMIYA ET AL.	
	Examiner	Art Unit	
	SCARLETT GOON	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *21 August 2007 and 23 October 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed on 10 July 2007 in which claim 3 was currently amended and claims 6 and 7 were newly added, is acknowledged.

Claims 1-7 are pending in the instant application.

Priority

This application is a National Stage entry of PCT/JP05/00979 filed on 26 January 2005 and claims priority to Japan foreign application 2004-017024 filed on 26 January 2004. A certified copy of the foreign priority document in Japanese has been received. No English translation has been received.

Information Disclosure Statement

The information disclosure statements (IDS) dated 21 August 2007 and 23 October 2007 complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Accordingly, they have been placed in the application file and the information therein has been considered as to the merits. Reference 1 of IDS dated 21 August 2007 was not considered because an English translation was not provided.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It was not executed in accordance with either 37 CFR 1.66 or 1.68.

In this case, the oath or declaration is defective because each inventor did not sign the oath or declaration.

Claim Objections

Claim 2 is objected to because of the following informalities: "Claim" is spelled incorrectly as "cliam". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "medicament" in claims 1-7 renders the claims herein indefinite. The recitation of "medicament" is unclear as to whether the claim is drawn to a composition or to a method of use. In order to further expedite the prosecution of this application, the recitation "medicament" will be interpreted as a pharmaceutical composition.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for therapeutic treatment of some specific pain (as further discussed below on pages 6-9 herein), does not reasonably provide enablement for the prophylactic treatment of pain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

All of the *Wands* factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The rejected invention is drawn to a medicament for prophylactic treatment of pain, which comprises ginsenoside Rb_1 as an active ingredient.

Relative skill of those in the art: The relative skill of those in the art is high.

Breadth of claims: The claims specifically include the medicament for prophylactic treatment of pain.

State of the prior art/Predictability or unpredictability of the art: A prophylactic is a preventive measure (PTO-892, Ref. U). As a medication or treatment, it is designed and used to prevent a disease. The skilled artisan would view that the treatment to prevent pain totally or absolutely, or not even occurring for the first time, is highly unlikely.

Amount of guidance/Existence of working examples: The specification provides examples for therapeutic treatment of pain after onset. However, there are **no** working examples present which show that the medicament can be used for prophylactic treatment of pain.

Lack of a working example is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.

Quantity of experimentation necessary: In order to practice the invention with the full range of all possible treatment methods beyond those known in the art, such as using ginsenoside Rb_1 as a medicament for prophylactic treatment of pain, one skilled in the art would need to undertake a novel and extensive research program to show that the medicament comprising ginsenside Rb_1 prevented the pain from occurring. Because this research would have to be exhaustive, and because it would involve such a wide and unpredictable scope of use, it would constitute an undue and unpredictable experimental burden.

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the use of the claimed medicament for the prophylactic treatment of pain, as recited in the instant claims.

Genetech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors as discussed above, e.g., the amount of guidance provided, the predictability of the art and the lack of working examples, Applicants fail to provide information sufficient to practice the claimed invention for use of the medicament for prophylactic treatment of pain.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for therapeutic treatment of hyperalgesia resulting from neuropathic pain, does not reasonably provide enablement for the treatment of any type of pain in claim 1, or any type of chronic or neuropathic pain (see claims 2-3 for example). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546

(BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

All of the *Wands* factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The rejected invention is drawn to a medicament for prophylactic and therapeutic treatment of pain, and more specifically, chronic pain or neuropathic pain, which comprises ginsenoside Rb_1 as an active ingredient.

Relative skill of those in the art: The relative skill of those in the art is high.

Breadth of claims: The claims specifically include the medicament for therapeutic treatment of pain, chronic pain and neuropathic pain. Pain, and even more specifically, chronic pain and neuropathic pain, arise from a wide range of conditions, such as that arising from tissue damage, inflammation, nerve damage, diabetes, or even cancer, thereby covering a large scope.

State of the prior art/Predictability or unpredictability of the art: The treatment of pain is a complex art due to the fact that pain can be caused by many different disorders, and no one treatment is universally useful for the treatment of pain. In particular, pain is divided into neuropathic and nociceptive categories, representing pain arising from a disorder of the nervous system and pain arising from a painful stimulus to the nerves, respectively. Chronic pain poses an additional challenge. Most often, acute

pain is nociceptive, whereas chronic pain can be nociceptive, neuropathic, or mixed in origin (Nicholson, abstract, PTO-892, Ref. V). Furthermore, as described by Woolf *et al.* (PTO-892, Ref. W), drugs used to treat nociceptive pain, including non-steroidal anti-inflammatory drugs and opiates, are often ineffective against neuropathic pain, such as that arising from nerve injury or diabetes, and vice versa (p. 1959, second column, second paragraph). Additionally, according to Woolf *et al.*, "There is no treatment to prevent the development of neuropathic pain, nor to adequatley, predicatably, and specifically control established neuropathic pain." (p. 1959, second column, third paragraph).

Amount of guidance/Existence of working examples: The instant specification provides an example for a sciatic nerve ligation injury model for neuropathic pain. Additionally, examples are provided that indicate the effectiveness of ginsenoside Rb_1 against hyperalgesia, but not allodynia. It is noted that allodynia arises from nociceptive pain. However, hyperalgesia pain can be caused by damage to nociceptors or peripheral nerves.

Quantity of experimentation necessary: In order to treat chronic pain or neuropathic pain using ginsenoside Rb_1, one skilled in the art would need to undertake a novel and extensive therapeutic research program to show that the composition comprising ginsenside Rb_1 is effective against all etiologies of neuropathic pain and chronic pain, which encompasses both neuropathic pain and nociceptive pain. Because this research would have to be exhaustive, and because it would involve such a wide

and unpredictable scope of use, it would constitute an undue and unpredictable experimental burden.

Genetech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the use of the claimed medicament for the treatment of pain, specifically chronic pain and neuropathic pain, as recited in the instant claims.

Therefore, in view of the *Wands* factors as discussed above, e.g., the amount of guidance provided, the predictability of the art and the lack of working examples, Applicants fail to provide information sufficient to practice the claimed invention for use of the medicament for treating all pain.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by WIPO publication no. WO 02/069980 A2 by Sengupta *et al.* (IDS dated 21 August 2007).

Sengupta *et al.* discloses the use of panaxadiol, preferably naturally-occurring ginsenoside Rb_1, for the treatment of conditions requiring stimulation of angiogenesis. Furthermore, a medicament comprising a panaxadiol ginsenoside, preferably Rb_1, is manufactured for the treatment of a human or other subject by stimulation of angiogenesis (p. 3, lines 18-21).

With respect to the art rejection above, it is noted that the reference does not teach that the composition can be used in the manner instantly claimed, for therapeutic treatment of chronic or neuropathic pain. However, the intended use of the claimed composition does not patentably distinguish the composition, per se, since such disclosed use is inherent in the reference composition. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting.

With respect to instant claim 5, the recitation "The medicament...is an α_{2A}-adrenergic receptor-agonistic medicament comprising..." is considered an inherent property of the compound. When, as here, the prior art appears to contain the exact same ingredients and applicant's own disclosure supports the suitability of the prior art composition as the inventive composition component, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562

F.2d 1252, 195 USPQ 430 (CCPA 1977). It is incumbent upon the applicant to provide evidence or comparative data to the contrary.

Thus, the medicament comprising ginsenoside Rb_1, disclosed by Sengupta *et al.*, anticipates claims 1-7.

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by published journal article by Choi *et al.* (IDS dated 23 October 2007).

Choi *et al.* teach antinociceptive effects of ginsenosides injected intracerebroventricularly or intrathecally in a substance P-induced pain model. Ginsenosides administered systemically, intracerebroventricularly or intrathecally are involved in the regulation of nociception in various pain models (p. 1001, introduction). Substance P, located in the primary nerve ending, is known as an important neurotransmitter for the pain transmission (p. 1002, first paragraph). The nociceptive behavior induced by substance P injected intrathecally has been used as a pain model. In their work, Choi *et al.* examined whether ginseosides have the antinociceptive effect on the nociceptive behavior elicited by substance P injected spinally. All the ginsenosides used for injection, except for ginsenoside Rd, were dissolved in sterile saline (0.9% NaCl solution), while ginsenoside Rd was prepared in saline containing 20% dimethylsulfoxide, which was used as a vehicle control (p. 1002-1003, bridging paragraph between the pages). Choi *et al.* injected 50 mg of ginsenosides Rb_1, Rb_2, Rc, Rd, Re, Rf, Rg_1 and Rg_3 intracerebroventricularly or intrathecally into mice and observed their nociceptive behavioral responses (p. 1002, column 2, first full

paragraph). Their results suggest that intrathecal treatment with Rb_1, Rb_2, R_d or R_f exerted an inhibitory action against substance P-induced nociceptive behavior (p. 1003, subheading "Discussion"). Furthermore, Rb_1, Rb_2, Rd or Rf treated intrathecally produced antinociception in the substance P-induced pain model.

With respect to instant claim 5, the recitation "The medicament...is an α_{2A}-adrenergic receptor-agonistic medicament comprising..." is considered an inherent property of the compound. When, as here, the prior art appears to contain the exact same ingredients and applicant's own disclosure supports the suitability of the prior art composition as the inventive composition component, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). It is incumbent upon the applicant to provide evidence or comparative data to the contrary.

Thus, the intrathecal ginsenoside Rb_1 solution, disclosed by Sengupta *et al.*, anticipates claims 1-7.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-

270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623

/SCARLETT GOON/
Examiner
Art Unit 1623